REMARKS

Claims 27-43 and 45-58 have been rejected and remain pending. In addition, claims 27 and 43 have been amended to recite that the nucleic acid sequence is upstream of a nucleic acid encoding a viral polypeptide. Applicants' specification fully supports these claim amendments. For example, page 26, lines 3-19 disclose inserting the sequence encoding the marker upstream of a nucleic acid encoding a viral polypeptide (e.g., between the H and L protein coding sequences). Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 27-43 and 45-58.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 27-43 and 45-58 under 35 U.S.C. § 112, first paragraph, alleging that "the specification, while being enabling for using a Measles virus (MV) comprising a nucleic acid, encoding a heterologous marker polypeptide, inserted at the 5' end of viral genes, e.g., N, P, L, etc., to monitor gene expression of viral genes, does not reasonably provide enablement for using any Paramyxoviridae virus comprising a nucleic acid, encoding a heterologus marker polypeptide, inserted at the 3' end of viral genes, e.g., N, P, L etc., to monitor gene expression of viral genes in an organism." Specifically, the Examiner stated that when "the nucleic acid encoding the heterologous polypeptide is located at the more distal end from the 5' viral promoter, the expression of said heterologous polypeptide could be insufficient such that said polypeptide cannot be detected in a biological fluid and the non-detection of said polypeptide does not correspond to the amount of gene expression of viral genes 5' to the nucleic acid encoding said heterologous polypeptide." The Examiner also stated that the "specification fails to provide adequate guidance and evidence that any virus in the family of Paramyxoviridae would have the same type of gradient gene expression within said viral genome and detection of heterologous polypeptide in a biological fluid can be used as an indicator for the amount of viral gene expression in a virus infected cells within an organism." In addition, the Examiner stated that "one skilled in the art at the time of the invention would not know how to use the claimed

Paramyxoviridae virus comprising a nucleic acid encoding heterologous polypeptide having MW less than 10 kD."

Applicants respectfully disagree. Applicants' specification fully enables the previous claims. To further prosecution, however, claims 27 and 43 have been amended to recite that the nucleic acid sequence is upstream of a nucleic acid encoding a viral polypeptide. A person having ordinary skill in the art reading Applicants' specification would have been able to make and use the presently claimed invention. In fact, given Applicants' specification and the common genome structure of Paramyxoviridae viruses (e.g., negative stranded RNA viruses), a person having ordinary skill in the art would have been able to insert a nucleic acid sequence encoding a heterologous polypeptide upstream of nucleic acid encoding a viral polypeptide. In addition, a person having ordinary skill in the art would have been able to use these viruses to monitor gene expression of virally encoded nucleic acid without undue experimentation. Again, Paramyxoviridae viruses have a particular genome structure that results in a gradient of viral gene expression. See, section 4 on page 26 of Applicants' specification.

With respect to the Examiner's assertion that a person having ordinary skill in the art would not know how to use the claimed Paramyxoviridae virus comprising a nucleic acid encoding heterologous polypeptide having a molecular weight less than 10 kD, Applicants' respectfully submit the following. Page 14, lines 4-16 teach that a heterologous polypeptide can have a molecular weight below 10 kD. In addition, the section extending from page 15, line 3 to page 18, line 29 provides multiple examples of heterologous polypeptides such as cleavage products, activation peptides, inactivation peptides, and synthetic non-human peptides. Clearly, a person having ordinary skill in the art reading Applicants' specification would have been able to make and use a virus containing a nucleic acid encoding a heterologous polypeptide that is biologically inactive and has a molecular weight less than 10 kD without undue experimentation.

In light of the above, Applicants respectfully request withdrawal of the rejections of claims 27-43 and 45-58 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 43, 46-54, and 58 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,175,099 (the '099 patent) in view of U.S. Patent No. 5,698,530 (the '530 patent). Specifically, the Examiner stated that claims 43, 46-54, and 58 "are directed to a Paramyxoviridae virus such as a SV40 virus, comprising a nucleic acid sequence encoding a heterologous polypeptide which is a biologically inactive polypeptide, such as a tumor antigen including CEA." The Examiner also stated that the '099 patent "teaches construction of replicable expression vectors, such as retrovirus vector and SV40 vector, comprising a hybrid gene for producing fusion proteins which are secreted in membraneous particles budding from cell membrane in to the culture medium or extracellular space, a process known as retrovirus-mediated secretion, and the hybrid gene contains a proteolytic cleavage site joining a modified retrovirus gas gene and a heterologous gene (e.g. abstract, column 4)"; while the '530 patent "teaches that CEA is a tumor-associated antigen that has been used clinically as a marker following primary tumor resection and anti-CEA antibodies have been used in diagnostic imaging of primary colon tumors (e.g. column 1)." In addition, the Examiner concluded that it "would have been obvious for one of ordinary skill in the art at the time of the invention to substitute the heterologous gene as taught by Wills [the '099 patent] with the nucleic acid encoding CEA as taught by Scholm [the '530 patent] because both the heterologous gene and nucleic acid encoding CEA are DNA sequences and CEA is heterologous to the retrovirus or SV40 vector and Scholm [the '530 patent] teaches expressing CEA is [sic] a viral vector, i.e., vaccinia vector." Lastly, the Examiner stated that one "having ordinary skill in the art at the time the invention was made would have been motivated to do so in order to produce fusion protein comprising CEA that is secreted in membraneous particles by using SV40 vector and purification of said protein and use in therapeutics as taught by Wills [the '099 patent] with reasonable expectation of success."

Applicants respectfully disagree with this rejection. Claims 43, 46-54, and 58 recite Paramyxoviridae viruses. Retroviruses and SV40 viruses are not Paramyxoviridae viruses. In addition, at no point do the cited references teach or suggest a Paramyxoviridae virus as

presently claimed. Thus, the cited reference do not render the presently claimed invention obvious.

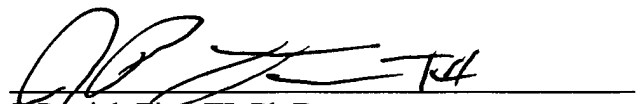
In light of the above, Applicants respectfully request withdrawal of the rejection of claims 43, 46-54, and 58 under 35 U.S.C. §103(a).

CONCLUSION

Applicants submit that claims 27-43 and 45-58 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: November 3, 2003



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